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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,450	09/01/2005	Marc Donath	4614-0160PUS1	5584

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EXAMINER	
DANG, IAN D	

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
05/14/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/517,450	DONATH, MARC	
	Examiner	Art Unit	
	IAN DANG	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01/25/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

As indicated in the interview summary filed 11/02/2007, the previous office action was made non-final.

Status of Application, Amendments and/or Claims

The amendment of 25 January 2008 has been entered in full. Claims 1-14 have been cancelled and claim 21 has been amended. Claims 22-26 have been added.

Claims 15-26 are under examination.

Rejections Withdrawn

35 USC § 112, First paragraph (Written Description)

Applicant's response and arguments filed on 01/25/2008 have overcome the rejection of claims 15-21 under 35 USC 112, First paragraph (Written Description). The rejection of claims 15-21 under 35 USC 112, First paragraph (Written Description) has been withdrawn.

35 USC § 112 (New Matter)

Applicant's response and arguments filed on 01/25/2008 have overcome the rejection of claims 15-21 under 35 USC 112, First paragraph (New Matter). The Examiner has found support for the recited "dose of 0.1 to 1000mg" at page 13, lines 13-15 of the specification. The rejection of claims 15-21 under 35 USC 112, First paragraph (New Matter) has been withdrawn.

Rejections maintained

Claim Rejections - 35 USC § 112, First paragraph (Enablement)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-21 remain rejected under 35 U.S.C. 112, first paragraph, and the newly added claims 22-26 are also rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for (1) restoring glucose-stimulated insulin secretion in β islet cells exposed to high glucose *in vitro* by culturing the cells with IL-1Ra and PDTC (figure 6, page 6), (2) measuring the expression of IL-1Ra in human islets and observing its down regulation in human islets from patients with type 2 diabetes (figure 7, page 6), and (3) inhibiting β islet cell apoptosis and restoring β islet cell function in vitro comprising culturing the cells with IL-1Ra (figure 9, page 7; page 35-36), does not reasonably provide enablement for a method of treating or prophylactically suppressing type 2 diabetes, the method comprising administering to a mammal in need thereof a medicament comprising a sufficient amount of anakinra. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims. The rejection is maintained for the reasons already of record on page 5-10 of the office action mailed 11/02/2007.

Although Applicants have partially overcome the enablement rejection regarding the in vivo methods, the enablement rejection is maintained for a prophylactic treatment.

Prophylactic Treatment

At page 8 of the response, Applicants indicate that in both the Office Action and the Interview of October 16, 2007 the Examiner raised concerns about use of the term "prophylactically" in claim 15. While Applicant is aware of the USPTO standard reluctance to allow claims that encompass "prophylactic" treatment, Applicant submits that such claims are

entirely proper in the present case. Enclosed as Exhibit 6, is a publication to Maedler et al. (which includes the present inventor as a co-author) which reports the results of tests on the use of IL-1ra to protect cultured human islets from the deleterious effects of high glucose. As shown in, for example figure 4g, IL-1ra prevented human 13-cell apoptosis at high glucose concentrations, evidencing the protecting role of anakinra in preventing type-2 diabetes. In other words, these results show the prophylactic benefit of the method of the present invention, as well as the benefit in preventing type-2 diabetes disease progression.

In addition, Applicants indicate that Exhibit 7 is an abstract of an article/presentation by Sauter et al. at the American Diabetes Association meeting in 2007 which also reports on tests which show that the treatment with IL-Ira in combination with a high fat diet prevented the onset of diabetic symptoms - i.e. the treatment had a prophylactic effect.

Applicants' arguments and evidence presented in Exhibits 6 and 7 have been considered but are not found persuasive. Although the reference by Maedler et al. provides evidence that IL-1Ra protects cultured human islet cells from deleterious effects of glucose, Applicants is not enabled for a method of prophylatically suppressing type 2 diabetes in a mammal because the protection of islet cells is not equivalent to the prophylactical suppression of type 2 diabetes. The reference does not provide any evidence that the protection of islet cells will not lead to type 2 diabetes in a mammal as indicated with the recitation "of prophylatically suppressing type 2 diabetes in a mammal." As disclosed at page 10 of the Office action mailed 11/02/2008, It is noted that the term "prophylactically suppressing type 2 diabetes" has been interpreted by the Examiner as meaning that an activity will not occur, i.e. type 2 diabetes will not occur.

In addition, the protection of islet cells by IL-1Ra is not commensurate in scope with prophylatically suppressing type 2 diabetes because islet cell biological activity represents only one component of type 2 diabetes. Type 2 diabetes is a complex disease with a wide array of abnormal metabolic disorders including insulin metabolism and kidney functions. The reference focuses on the biological activity of islet cells and does not provide any evidence for other cellular metabolism associated with type 2 diabetes. Finally, neither Applicants nor the reference have provided a nexus between the effects of cultured human islets with those of treatment of type 2 diabetes in a mammal.

In addition, the abstract disclosed in Exhibit 7 indicates that high fat diet mice (hyperglycemic mice), which were treated with IL-1Ra, showed improved glucose tolerance. While the reference indicates that IL-1Ra improved glucose tolerance in hyperglycemic mice, the study does not provide any evidence that IL-1Ra can treat or prophylactically suppress type 2 diabetes. As disclosed above, term "prophylactically suppressing type 2 diabetes" has been interpreted by the Examiner as meaning that an activity will not occur, i.e. type 2 diabetes will not occur. The reference has not provided any evidence that hyperglycemic mice with improved glucose tolerance when administered IL-1Ra is equivalent to the fact that type 2 diabetes will not occur. More specifically, Applicants have not disclosed that impaired glucose tolerance was prevented in ALL mice at all time points. In addition, Applicants have not provided the nexus between the prevention of impaired glucose tolerance in hyperglycemic mice to that of treatment of type-2 diabetes these mice. In addition, the reference indicates that the study indicates a potential role for IL-1Ra in the future treatment of diabetes but not specifically to type 2 diabetes. Furthermore, the reference indicates that IL-1ra protects animal from high fat diet induced diabetes, but does not address any symptoms associated with diabetes nor any other types of diabetes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15-17 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Boone et al. (US Patent No. 6,294,170, filed August 07, 1998) in view of Thompson et al. (US Patent No. 6,159,460, filed August 18, 1994) for the reasons set forth at pages 10-11 of the office action mailed 11/02/2007.

At page 9 of the response, Applicants argue that Boone et al. says nothing at all about the use of anakinra for the treatment of type-2 diabetes. The differences between the two types of diabetes are significant, and a treatment useful for one type of diabetes cannot be considered prima facie obvious for the use in treating the other type of diabetes.

In addition, Applicants allege that the term "insulin diabetes" as utilized in Boone et al. refers exclusively to type-1 diabetes - i.e. insulin dependent diabetes. Type-1 diabetes is an auto-immune disease with the involvement of cytokines, including interleukin-1.

Moreover, Applicants argue that the Boone et al. reference cited by the Examiner which relates to treatment of insulin diabetes is completely silent with respect to the use of anakinra for type-2 diabetes and prior to the present invention there was no motivation for one skilled in the art to consider treating type-2 diabetes with interleukin-1 receptor antagonists such as anakinra. Applicants indicate that it was surprising to the present inventor to find that interleukin-1 was implicated in type-2 diabetes.

Finally, Applicants argue that Thompson et al., cited by the Examiner, similarly only refers to the treatment of interleukin-1 mediated diseases, including insulin diabetes (column 2, line 46), and is silent with regards to any treatment of type-2 diabetes.

Applicants' arguments have been considered but have not been found persuasive. The reference by Boone et al. teaches diabetes and mentions "e.g. insulin diabetes." Since the reference by Boone uses "e.g.", Boone implies that this is only one example of diabetes he intends to include and that the term "insulin diabetes" would encompass type-2 diabetes as well. Given the state of the art at the time of filing, there are only 2 types of diabetes: type 1 and 2. In the event that Boone intended to mean only type 1, he would have likely said disclosed type -1 diabetes (i.e. type 1).

Regardless of the intention of Boone's statement, claim 15 is drawn to a method of prophylactically suppressing type 2 to a mammal in need. One of skill in the art would expect that every mammal would be in need of this, since no mammal would want to have diabetes. Therefore, any method of administering the compound for any reason or any population would meet this limitation.

Finally, although the reference by Thompson is silent regarding type-2 diabetes, the disclosure of "insulin diabetes" would encompass type 2 diabetes. Thus it would be obvious that the treatment of IL-1 mediated disease with IL-1RA would include type 2 diabetes.

New Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Thompson et al., (US patent No. 6,159,460, filed August 18, 1994).

The invention is drawn to a method of treating or prophylactically suppressing type 2 diabetes comprising administering to a mammal in need thereof a medicament comprising a sufficient amount of anakinra. The medicament anakinra of the claimed method is adapted for parenteral administration.

Thompson et al., (US patent No. 6,159,460, filed August 18, 1994) teach a method for the treatment of interleukin-1 mediated diseases in a patient by administering IL-1ra (also named anakinra) formulations containing IL-1ra via an intraarticular, subcutaneous, or intramuscular route (or parenteral administration) (column 9, lines 52-54; Asbtract) meeting the limitations of claims 15 and 16.

Although the reference is silent regarding a method of prophylactically suppressing type 2 to a mammal in need, one of skill in the art would expect that every mammal would be in need of this, since no mammal would want to have diabetes. Therefore, any method of administering the compound for any reason or any population would meet this limitation.

Conclusion

No claim is allowed.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IAN DANG whose telephone number is (571)272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang
Patent Examiner
Art Unit 1647
May 8, 2008

/Robert Landsman/
Primary Examiner, Art Unit 1647